DETAILED ACTION

Status of Claims

Claims 1-16, 93-101, 106, 107, 112-133, 138-159, 162, 164-165, 167, 169, 171, 173-175, 177, 181-186, 188, and 193-197 are pending.

Claims 12-16, 93-101, 106, 107, 112-133, 138-140, 142-159, 162, 165, 167, 171, 175 and 196-197 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species, there being no allowable generic or linking claim.

Claims 17-92, 102-105, 108-111, 134-137, 160-161, 163, 166, 168, 170, 172, 176, 178-180, 187, 189-192 and 198 have been cancelled.

Claims 1-11, 141, 164, 169, 173, 174, 177, 181-186, 188 and 193-195 are under consideration in this Office Action.

Withdrawn Objection and Rejections

In view of applicants' arguments and amendments to the claims, the 35 USC 112, second paragraph rejections have been withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-11, 141, 164, 169, 173, 174, 177, 181-186, 188 and 193-195, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record as reiterated below.

Written Description Rejection

A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California

v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiefs V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993.

The claimed invention is drawn to a positionally addressable array comprising a plurality of different substances on a solid support, with each different substance being at a different position on the solid support, wherein the density of the different substances on the solid support is at least 100 different substances per cm2, and wherein the plurality of different substances comprises 61 purified active kinases or functional kinase domains thereof of a mammal, 61 purified active kinases or functional kinase domains thereof of a yeast, or 61 purified active kinases or functional kinase domains thereof of a Drosophila.

The specification fails to provide an adequate written description of 61 purified kinase and functional domains thereof from any organism such as mammals. The specification provides general statements of these various kinases in an organism which are not a detail description of the invention. The detail description in the specification (Example I, page 27) describes the 122 kinase genes specifically from the yeast genome, not from the broad claimed any kinase from any type of mammals or Drosophila or functional domains thereof. A written description

of a single species would not be a written description for the genus as claimed. At the time of applicants' invention kinases in any mammals included in the huge scope of the claim has not been fully characterized such that it has been positioned in an array without denaturing the purified protein. A skilled artisan recognizes that one cannot rule out the possibility that kinases other than the desired enzyme can contaminate any type of purification preparations. Notwithstanding this, the kind/type and preparation of a substrate compatible with the purified protein is also a factor to consider for a purified protein to be active in an array. Furthermore, "although most of the kinases were active in [our] assays, several were not. Presumably, our preparations of these latter kinases either lack sufficient quantities of an activator or were not purified under activating conditions. For example, Cdc28 which was not active in [our] assays, might be lacking its activating cyclins. For the case of Hog1, cells were treated with high salt to activate the enzyme…." (paragraph [0161] of the instant specification, publication no. 20030207467).

Attention is also drawn to the numerous prior art cited by applicants, inter alia, the Anderson reference, which teaches the numerous unforeseeable factors of a purified kinase positioning in an array.

Anderson states that:

> …protein microarrays have still not found widespread use, in part because producing them is challenging. Historically, it has required the high-throughput production and purification of protein, which then must be spotted on the arrays. Once printed, concerns remain about the shelf life of proteins on the arrays.

Shaw et al (Drug Discovery and Development, Exhibit B)

concords with the statement that:

> "[i]t was first thought that protein biochips would just be an extension of DNA microarrays, and that hasn't exactly panned out," says Bodovitz. That's because proteins have proven to be much trickier to work with in array format than their genomic counterparts. First of all, there are issues of stability. Membrane proteins, for example, make up the majority of potential drug targets, but they're particularly challenging to stabilize. Then there's the choice of immobilization technique, which determines how well the target protein presents itself to the capture agent, and the problem of nonspecific binding. And of course, proteins are inherently unstable outside their natural habitat of living cells, making them much more challenging than DNA to tag and manipulate.

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures and formulas to show that the invention is complete. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQM 1961, 1966 (Fed. Cir. 1997); MPEP 2163. Herein, kinase has been described only in words. The characterization of the different kinases from one organism to another from the numerous kinases and numerous

organisms has not been adequately described to distinguish one from the other. To date only a few organisms are fully characterized and the kinase region has not been fingerprinted in a partly or even fully characterized gene. The description lacks structural characterization of a purified kinase as generically claim. It does not distinguish one kinase from another and/or one organism from another positioned in any kind/type of substrate array and reasonably expect the purified kinase to retain its active form.

Response to Arguments

Applicants submit that kinases and functional kinase domains from yeast, mammals and Drosophila were a well characterized group of proteins that were generally known, understood to be well conserved in structure and function, easily identified, and readily prepared and assayed by those of ordinary skill in the art on the priority date of the present application. Thus, such proteins were well known to those of ordinary skill in the art, and hence, a re-description of such proteins is not required under Capon.

In reply, the claims are not drawn only to the alleged known, well characterized kinases from yeast, mammals and

Drosophila or functional domain thereof. Rather, to a kinase array for all or any kind of kinase from e.g., mammals or functional domain immobilized in every conceivable manner on any kind of solid support. If an appellant choose to rely upon general knowledge in the art to render his disclosure enabling, the appellant must show that anyone skilled in the art would have actually possessed the knowledge, In re Lange (CCPA 1981) 644 F2d 856, 209 USPQ 288, or would reasonably be expected to check the source which appellant relies upon to complete his disclosure and would be able to locate the information with no more than reasonable intelligence. Herein, there is no explicit description of the generic claim array containing kinases from any kind of e.g., mammals (except for humans as per the newly submitted Schweitzer declaration), let alone to the functional domain thereof. Claims drawn to the use of known chemical compounds must have a corresponding written description only so specific as to lead one to that class of compounds. In re Herschler (CCPA 1979) 200 USPQ 711.

Applicants submit that the level of skill and knowledge relating to protein kinases and their functional domains was very high on the priority date of the present application and a person of ordinary skill in the art would readily understand

that indeed, Applicants were clearly in possession of a positionally addressable array comprising 61 purified active kinases or functional kinase domains thereof of a mammal, yeast or Drosophila.

In reply, the level of skill and knowledge in the art is high so also the unpredictability in the gene art. This is demonstrated by no less than applicants for the very specific yeast ORF genes containing kinase, not the functional domain thereof. Applicants state at e.g., page 32, lines 14-17:

> "……14 of 15 119 GST::kinase samples were not detected by immunoblotting analysis. Presumably, these proteins are **not stably overproduced** in the pep4 protease-deficient strain used, or **these proteins may form insoluble aggregates that do not purify using our procedures**……."

Please see also the various prior art concording with applicants' findings above. For example, Anderson states:

> …protein microarrays have still not found widespread use, in part because producing them is challenging. Historically, it has required the high-throughput production and purification of protein, which then must be spotted on the arrays. Once printed, concerns remain about the shelf life of proteins on the arrays.

Applicants state that the specification describes the use of positionally addressable arrays containing proteins and functional domains of the proteins from organisms including mammals, yeast and Drosophila (published [0058]); and provides a working example describing the production of a protein chip containing over 100 functional yeast kinases and yeast kinase domains (See Example I).

In reply, the detail description of the yeast array as described in Example I is not controverted. The issue is e.g., an array containing not only yeast but any type of mammal kinase and/or Drosophila (sequence or non-sequence) (and at least 61 kinase in an array).

There is nothing in the description or any prior art teachings of an array containing an immobilized kinase from yeast, mammals and Drosophila or functional domain thereof. It does not describe that the 61 kinase present in yeast can be extrapolated or are similarly present to the different numbers and kinds of kinases found in any kind of mammals or Drosphila.

Attention is again directed to the different prior art cited above as to the high unpredictability in the art for an array containing protein such as kinase.

Claim Rejections - 35 USC § 112

Enablement Rejection

Claims 1-11, 141, 164, 169, 173, 174, 177, 181-186, 188 and 193-195, as amended, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for yeast protein' kinases of the Ser/Thr and tyrosine kinase family, does not reasonably provide enablement for the broad scope of an array of 61 kinases and functional domain kinase from an organism as mammal, yeast or Drosophila. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons as repeated below.

The claimed array comprises a broad genus of compositions. The claimed different substances encompass any members of the protein kinase from the organism of mammal, yeast, or Drosophila which is broader than the enabling disclosure. The claimed array represents enormous scope because the claims do not place any limitations on the kind, number and/or length of kinase either

singly from one family of organism or a combination(s) from the different numerous recited organisms. The instant specification is directed to an array comprising a plurality of different yeast protein kinase, specifically 122 different yeast protein' kinases of the Ser/Thr and tyrosine kinase family members (see specification: example I, pg. 27, line 19 thru pg. 35, line 20; example II, pg. 41, line 19 thru pg. 43, line 6). The specification does not provide reasonable assurance to one skilled in the art that the 61 kinases found in the yeast could be found in any or all of the organisms such as mammals especially the functional domain thereof. It is not apparent from the specification whether the same number of kinases or the kind of kinases or functional domain thereof can be found in any other organisms and made into an array. It is not apparent from the disclosure as to the functional domain of the kinase and the specific function attributed to said kinase positioned on the array. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. In a highly unpredictable art, as biotechnology, where one cannot predict whether one species would be predictive to the huge scope of the claim, one cannot make a priori statement without any experimental studies. Factors such as the compatibility of the array with the

substrate and compounds disposed therein, the compounds (kinases) itself and other unpredictable variables can affect the active form of any kinase. Thus, one cannot predict from a single species its correspondence or extrapolation to the genus, as claimed.

Response to Arguments

Applicants cite the Schweitzer Declaration at pages 3-4, section 8, the Snyder Declaration and Replies to the Office Action filed December 21, 2007, and April 20, 2009 to support their enablement position. It is asserted that the replies and declaration show that protein kinases and functional kinase domains used in the claimed positionally addressable arrays were at the time this application was filed, all well-known, and well-characterized. Reference was made to the Hunter and Plowman reference.

In reply, as stated above the claims are drawn to an array of the well-known and well-characterized kinases in yeast and etc. and not solely to the well-known and characterized yeast, per se.

Hunter like the specification is drawn only to kinase in yeast, which is not present in an array. Mammals or Drosophila has not been described by Hunter or taught that the well known kinase from yeast, let alone, the functional domain, applies to other kinases as in mammals or Droosophila.

Applicants further assert that it was also well known at the time of filing of this application that kinases are highly conserved such that homologs exist between yeast and many other organisms. See Manning et al., "The Protein Kinase Complement of the Human Genome," Science 298:1912-1934 (2002) at page 1913, first column, first paragraph (cited in Applicants' 6th SIDS submitted on April 20, 2009). Furthermore, the regulation of the different kinases and the phosphorylation motifs of substrates recognized by related kinases are often the same, indicating that they behave similarly biochemically. See id. Moreover, as the structure and function of kinases were known to be highly conserved, it was also known that human kinases can be substituted for yeast kinases, illustrating the highly conserved structure-function relationships known to exist for kinases on the priority date of the application. See Lee and Nurse, "Complementation used to clone a human homologue of the fission yeast cell cycle control gene cdc2," Nature 327:31-35 (1987)

(cited in Applicants' 6th SIDS submitted on April 20, 2009). Therefore, on the priority date of the present invention, the state of the art relating to protein kinases was extremely high and was such that a person of skill in the art, in the fields of for example, protein purification, proteomics and analysis, enlightened by the teaching of the specification would have appreciated that no more than routine experimentation would be required to make and use the claimed arrays containing purified active kinases or functional kinase domains from a mammal, yeast or Drosophila.

In reply, the arguments are not drawn again to kinase in yeast per se as well as to its properties or homologs thereof. Rather, the claim is to a kinase of yeast in an array. As Shaw et al stated above:

> "[i]t was first thought that protein biochips would just be an extension of DNA microarrays, and that hasn't exactly panned out," says Bodovitz. That's because proteins have proven to be much trickier to work with in array format than their genomic counterparts. First of all, there are issues of stability. Membrane **proteins**, for example, make up the majority of potential drug targets, but they're **particularly challenging to stabilize**. Then there's the **choice of immobilization technique**, which determines how well the target protein presents itself to the capture agent, and the **problem of nonspecific binding**. And of course, proteins are inherently unstable outside their natural habitat of living cells, making them much more challenging than DNA to tag and manipulate. (Emphasis added.)

While the kinases are alleged to be homologs the fact remains that purification the technique and other experimental conditions/steps for yeast would be different from any type of mammals. See applicants' disclosure at e.g., page 32, lines 14-17 as to the unpredictable or unexpected failure of obtaining purified yeast in the ORF region alone (i.e., not to its alleged homologs):

> "……14 of 15 119 GST::kinase samples were not detected by immunoblotting analysis. Presumably, these proteins are **not stably overproduced** in the pep4 protease-deficient strain used, or **these proteins may form insoluble aggregates that do not purify using our procedures**……." (Emphasis added.)

Applicants submit that methods useful for confirming kinase activity of the proteins on the claimed arrays are described in the specification and were otherwise well known as of the filing date of the present application (see e.g., Example 1 of specification). See also Snyder Declaration at pages 3-4, section 7. Thus protein kinases, functional kinase domains and methods of assaying these proteins, were well-known in the art on the priority date of the present invention.

In reply, Example I states that the tyrosine kinase family members do not exist although seven protein kinases that phophorylate have been reported. Applicants' arguments that array from any organisms are simple and straightforward are mere arguments, absent evidence to the contrary, which cannot be substituted for enabling disclosure.

Applicants state for enablement, a specification need not teach, and preferably omits, information that is well-known to those of ordinary skill in the art. See Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986); Lindemann Maschinetzfabrik v. American Hoist and Derrick, 730 F.2d 1452, 1463 (Fed. Cir. 1984); In re Wands, 8 USPQ2d 1400, 1402 (Fed. Cir. 1988).

In reply, the Federal Circuit has cautioned against over reliance on the assertion that everything needed to practice the full scope of the claims was "known in the art" and that a patent need not teach, and preferably omits, what is well known in the art. See Genentech Inc. v. NovoNordiskA/S, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997): "[T]hat general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the

omission of minor details does not cause a specification to fail to meet the enablement requirement .... It is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute adequate enablement." Herein the specification teaches the kinase of yeast only in the ORF region (not even of the full length yeast sequence. Do the kinase and its functional domain exist only in the ORF region and not in any other region(s) of the yeast gene?) Applicants point to nothing in the specification that would indicate to the contrary (i.e., kinase array of e.g., any mammal or Drosophila in any region of the full length sequence or unsequence protein).

Applicants rely upon the newly submitted Schweitzer Declaration, in addition to the Snyder declaration. Schweitzer is stated to describe the preparation of functional human protein kinase arrays using the teaching in the present specification. In addition, the functional human kinase domains used in the positionally addressable arrays prepared by Schweitzer that form the basis of the present claims were, on the priority date of the present application, well-known, well-characterized proteins with purified human kinases (see the Schweitzer Declaration, at page 3, section 8). As discussed in

detail in the Schweitzer Declaration at pages 4-7, sections 9-13, researchers enlightened by the information set forth in the specification, have used the homologies that were known to exist between human and yeast kinases, to informatically identify genes for human kinases and functional domains, clone these genes, express these genes in Sf9 insect cells, lyse the cells and purify the human kinases and functional domains. (See also Protein-Protein Interaction Profiling on Invitrogen ProtoArray TM High-Density Protein Microarrays, Application Note, Invitrogen page 2, column 2, paragraph 3 - 2, column 3, paragraph 1 (2005) (hereinafter "Protein-Protein Interaction Profiling," Exhibit B)). According to the Schweitzer Declaration, over 90% of protein kinases expressed and purified using the methods described in the specification were active as demonstrated by catalytic activity including autophosphorylation, wherein a protein kinase phosphorylates itself. See id.

In reply, that the Schweitzer declaration teaches the purification of kinase from humans is not controverted. The Schweitzer declaration describes kinase allegedly obtained from human not from any mammals or Drosophila. It is not clear from the Schweitzer declaration just which part of the present

disclosure has been applied from the yeast to the human kinase array, except to get its homology therefrom. The instant specification uses chip for its yeast array. Schweitzer does not teach a biochip.

Exhibit B presents a description for the human array which does not seem to fall or correspond to the description for yeast. Furthermore Exhibit C of the Schweitzer declaration states at page 1:

> The family of human protein kinases consists of more than 500 members of which only a fraction have been characterized to date. Much is still not known about the biological function of many kinases, the protein substrates that are phosphorylated by these kinases, or the roles of these kinases and substrates in disease..

Thus, Schweitzer has not extrapolated or predicted its findings to any other family o human protein kinases which consist of more than 500 members to which only a fraction has been characterized to date.

Claim Rejections - 35 USC § 102/§ 103

Claims 1-11, 141, 181-186, 188, and 193-195, as amended, are rejected under 35 U.S.C. 102(a) as anticipated by or, in the

alternative, under 35 U.S.C. 103(a) as obvious over Uetz et al (Nature, 2/10/2000) for reasons of record as reiterated below.

Uetz et al, throughout the reference, teach a protein array representing yeast genome encoded proteins (see Abstract of the reference). The reference teaches fusing roughly 6000 potential ORFs (genes) from yeast genome (which comprises approximately 6000 genes) (see page 623, left col., 1st paragraph. and page 624, left col., 2nd paragraph). Uetz teaches the yeast proteins were expressed in 96-well assay plates (page 624, left col., bottom of 2nd paragraph), which reads on a solid support of the addressable array of claim 1 because each well of the plates would have defined (or addressable positions). The reference also teach each of the protein encoded by a gene is expressed individually in individual wells of the plates as shown in Figure 1 of the reference (page 624), which reads on each protein being at a different position on a solid support of claim 1, for example. The claimed kinase present in the array would have been inherent to the yeast array taught by Uetz since yeast inherently contain kinase in its structure or would have been obvious to determine given the identified genome of yeast as taught by Uetz.

> Where the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same as is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. See In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972); In re Best 195 USPQ 430 (CCPA 1977).

Response to Arguments

Applicants state that Uetz does not disclose the claim arrays comprising purified kinases or functional kinase domains. Applicants assert that Uetz pg 623, col. 1, last paragraph - col. 2, first paragraph provides further evidence that the arrays in Uetz did not consist of purified proteins having kinase activity.

In reply, attention is again drawn to the disclosure of Uetz at e.g., paragraph bridging col.1 and col. 2 which recites a purified yeast ORF (referring to reference 7) which contains the kinase region):

> To examine protein activity in a format that allows the assay of every predicted ORF: we constructed an array of hybrid proteins. At least two general types of protein array may be envisioned:

> those composed of living transformants….. and those composed solely of **the purified proteins (7)**. The two-hybrid array used here is a set of yeast colonies derived from about 6,000 individual transformants…... (Emphasis added.)

Thus, Uetz discloses purified protein containing the same kinase from yeast. Even assuming that Uetz does not disclose (but Uetz does) a purified kinase as argued however, the unpurified ORF of the yeast containing kinase would be the same as the claimed purified one. A purified kinase obtained from the same source as yeast merely further characterizes the known kinase present in the yeast. Applicants' use of the word comprising does not preclude the other elements present in the kinase contain in the ORF region of the yeast. As applicants stated above:

> Kinases and functional kinase domains from yeast, mammals and Drosophila were a well characterized group of proteins that were generally known, understood to be well conserved in structure and function, easily identified, and readily prepared and assayed by those of ordinary skill in the art are known.

Applicants note that, even assuming the arrays disclosed in Uetz comprise 61 kinases, there is no disclosure in Uetz sufficient to render obvious the construction of an array of 61 kinases or functional kinase domains, in which the array

comprises kinases that are purified and active, as recited in present claim 1.

Applicants agree that the claims are drawn to an array but assert that the limitation purified and active recited in the claims is not a process limitation, but rather a characteristic of the components of the array.

In reply, as recognized by applicants, a purified kinase is but a further characteristics of the known (albeit, allegedly unpurified) compound. Thus, this further characterization does not make the compound, kinase any different but only further characterizes said known kinase. It is well settled that there can be no patentable invention where novelty does not exist, albeit all of the properties of said compositions were not previously recognized. (Please see further the above statements of applicants that these kinases are known).

Likewise, it is well settled in the art that where substance having medicinal properties is produced, it becomes an immediate consideration to prepare substances in as pure a form as possible. Claim for known substance which differs from prior art only in degree, as for example in purity, is not patentable. See Ex parte Steelmand and Kelly, 140 USPQ 189.

Most of applicants'' subsequent arguments rely on the responses filed on December 21, 2007 and the April 20, 2009 replies and the Snyder declaration. Applicants state that the following exemplary references describe the skepticism from those in the field regarding the **preparation** of protein arrays both before and after the time of filing of the present application, as well as some of the problems regarding **preparation of protein arrays** comprising large numbers of purified active proteins that **were overcome by the presently claimed invention**"); Schweitzer declarations and the reference to e.g., Anderson, all relate to the problems encountered into the making of the array and how the problems have been overcome. (Emphasis added.) However, as stated above and in the previous Office actions the claims are drawn to known kinases the immobilization thereof into a solid surface is well known in the art as taught by Uetz above.

Applicants state that the examiner appears to agree that kinases of the various organisms such as mammals, Drosophila and yeast were well known at the time of filing the application. This is in stark contrast to the Examiner's contrary position noted above with regard to written description and enablement of the presently claimed invention. While Applicants agree that

kinases of Drosophila, yeast and mammals were well known in the art at the time of filing the present application, it would not have been obvious to place these kinases on a positionally addressable array so that they were not only purified, but also active.

In reply, no contradiction exists in the rejections under obviousness and enablement/written description. These are two separate rejections. The enablement/written description are based on the lack of description for the broad claim genus and not to the yeast species containing kinase. This species is taught by the prior art which is included in the broad genus claim hence, anticipating or rendering obvious the broad genus claim. Applicants' further arguments relying on the Synder declaration as to method of making the array and Bussow are as stated above not commensurate with the claims, which recite simply the known kinases immobilized on solid support.

Claims 1-11, 141, 181-186, 188, and 193-195 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon (WO 95/35505) in view of Felder et al (USP 6458533) or Lafferty(USP 6972183) for reasons of record as repeated below.

Shalon discloses at e.g., page 12, lines 3-9:

> A microarray as an array of regions having a density of discrete regions of at least about 100/cm2, and preferably at least about 1000/cm2. The regions in a microarray have typical dimensions, e.g., diameters, in the range of between about 10-250 um, and are separated from other regions in the array by about the same distance.

Shalon discloses at e.g., page 30, line 30 up to page 32, line 15:

> Sheets of plastic-backed nitrocellulose where each microarray could contain, for example, 100 DNA fragments representing all known mutations of a given gene. The region of interest from each of the DNA samples from 96 patients could be amplified, labeled, and hybridized to the 96 individual arrays with each assay performed in 100 microliters of hybridization solution…… In addition to the genetic applications listed above, arrays of… enzymes…(were prepared].

Shalon discloses an array of enzymes and not kinase as claimed. However, Feder discloses:

Feder discloses at Example 18:

> Kinases are enzymes that attach a phosphate to proteins. Many have been shown to stimulate normal and neoplastic cell growth. Hence, compounds that inhibit specific kinases (but not all kinases) can be used to test whether the kinases are involved in pathology and, if so, to serve as starting points for pharmaceutical development… Each kinase has substrates that are partially identified, as short peptides that contain a tyrosine. Some of the kinase specificities overlap so that different kinases may phosphorylate some peptides equally but others preferentially. For the five kinases, 36 peptide substrates are selected that show a spectrum of specific and overlapping specificities.

Lafferty discloses at e.g., col. 31, lines 41-49 the conventionality of an array containing substrate-enzymes such as kinase.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use in the array of Shalon the enzyme kinase as taught by Feder. Feder teaches that kinase have been shown to stimulate normal and neoplastic cell growth. To use the kinase in the array of Shalon would lead one having ordinary skill in the art in determining the kinase in the array responsible for neoplastic or normal cell growth. Furthermore, as taught by Lafferty an array containing a kinase is known in the art. [See also applicants' admission in the response at page 17, of the 12/19/2006 REMARKS. Applicant states: compositions ***utilizing well-known and well-characterized classes of proteins***, as in the presently claimed invention].

Response to Arguments

Applicants argue that Shalon is primarily directed to arrays comprising polynucleotides (see Examples 1-3), and only mentions in passing that arrays comprising proteins and enzymes

could be constructed. Furthermore, Felder discloses preparation of arrays comprising peptides that are substrates for kinases, not arrays comprising the kinases themselves. Thus, Felder does not disclose the preparation of arrays comprising 61 purified active kinases or functional kinase domains thereof, as recited in present claim 1. With regard to Lafferty, Applicants note that the arrays disclosed therein are limited to enzymes expressed in expression library cells, and that Lafferty does not disclose the purification of these enzymes prior to placement on a solid support, as recited in the presently claimed invention. Applicants rely upon the Synder declaration as support that Lafferty does not disclose the purified enzyme on a solid support. Lafferty is alleged to use an impure clone of an enzyme repeatedly passed through a capillary array several times.

In reply, much of applicants' arguments are drawn to the method of making the array, which is not commensurate in scope with the claims. Shalon,as recognized by applicants above, only mentions in passing arrays. However, this “passing remarks” or inferential teachings suffice the findings of obviousness. In considering disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also

"inferences" which one skilled in the art would reasonably be expected to draw therefrom. In re Preda 159 USPQ 342.

The disclosure of Lafferty as discussed in the Synder declaration of passing the clone several times into a capillary array and producing an optically detectable signal would indicate a purified product to enable detection of the clone. The claimed number of 61 kinase is dependent upon the organism and location from which the kinase is contained. Thus, this number may be arbitrary considering that the kinase is only derived from the ORF region of yeast. To determine the number of kinases in an organism as yeast in a specific location would be within the ordinary skill in the art, as evidenced from the various well known kinases in a protein sequence.

Applicants cannot attack the references individually when the rejection is based on combination of references. Felder and Lafferty are employed for its disclosure of purified kinase, as claimed, not that it has to teach purifying the kinase prior to immobilization, otherwise it would be anticipatory rejection. Shalon teaches ORF containing kinase on an array but does not expressly teach, albeit implicitly, the purified kinase hence, the application of the secondary references Felder and Lafferty that renders the claim prima facie obvious. It would be within one having ordinary skill in the art at the time the invention

was made to position a known compound as kinase into an array, as taught by Shalon. There is nothing new and unobvious in mere positioning a known compound in e.g., array, when in nature these kinases are inherently arrayed or attached to e.g., a membrane, which would read on a substrate of an array.

Applicants assert that it was unexpected that kinases and functional kinase domains of these kinases could be purified and placed on a solid support to form an array, and that these kinases and kinase domains would retain their/kinase activity. As detailed in the Snyder Declaration and the Schweitzer Declaration, it is only after the guidance provided in the present specification that a person of ordinary skill in the art would consider it possible to generate the presently claimed arrays. As discussed above and in the Schweitzer Declaration, Applicants respectfully submit that at the time of filing of the present application, it was unexpected that kinases and functional kinase domains of these kinases could be purified and placed on a solid support to form an array, it was also unexpected that the purified kinases and functional kinase domains of these kinases would retain their activity when placed onto the array.

In reply, positioning of a known compound, be it purified or not, would be expected since the prior art, Shalon has successfully applied an enzyme protein in an array. There is nothing novel or unobvious of mere positioning or attaching a known compound, as kinase, as admitted by applicants above, in an array. The numerous advantages derived in arraying a known compound e.g., high throughput screening would provide motivation to one having ordinary skill in the art at the time of filing. One would have a reasonable expectation of success in immobilizing the yeast ORF containing kinase in an array as successfully made by Shalon and others in the prior art.

[Applicants' arguments above are mostly drawn to what appears to be the method of making an array immobilized with purified kinase. Perhaps, this might very well be where the novelty resides. It is therefore suggested that applicants draft/amend the claims to recite a method of making/using the array. The method claim may be an allowable subject mater in view of the alleged and argued unexpected results of the method of purifying and attaching kinase to a solid support.]

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

This application contains claims 12-16, 93-101, 106, 107, 112-133, 138-140, 142-159, 162, 165, 167, 171, 175 and 196-197 drawn to a non elected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639